

Testimony on June 28, 2006 to the House of Representatives, Energy and Commerce Committee, Health Subcommittee; Representative Nathan Deal, Chairman

Representative Deal, Ranking Member Brown, Mrs. Myrick and the Members of the Health Subcommittee: I am Ray DePaulo, Henry Phipps Professor and Chairman of the Department of Psychiatry at The Johns Hopkins University School of Medicine. I'm pleased to be invited here to speak about mental illness and brain disease. I have spent the last 30 years as a clinician, research, and teacher at Johns Hopkins focused on Depression and Bipolar Disorder, which are two of the serious brain diseases referred to as "mental illnesses". I will describe the prevalence and costs of these 2 conditions. I will explain why we are convinced that these are diseases of the brain (as surely as pneumonia and asthma are diseases of the lungs) and why I am confident that research will illuminate the molecular and structural pathways to these brain diseases and lead to much better ways to diagnose, treat and, in some cases, prevent these disabling diseases.

Major depression and bipolar disorder make up what are called mood disorders. The most recent estimate is that about 10% of Americans (and about 5% of adolescents) have had at least one episode of depression in their lifetime (Kessler et al, 2005). Most will have multiple episodes of depression and one in 10 of them will have one or more severe manic episodes. When depressed, patients experience a low, anxious, or apathetic change in their mood, inability to enjoy things that normally give them satisfaction or pleasure, a loss of energy, reduced ability to sustain attention & concentration, as well as a very negative change in their view of themselves and of the future. These symptoms, if untreated, last for several weeks up to a few years and like asthma or epilepsy once begun, they tend to recur. Most worrisome, patients with severe depressions often contemplate or attempt suicide. Of those who complete suicide most have depression and 90% have one or more diagnosable mental disorders based on information gathered about them prior to the suicide. Before he served in Congress, Abraham Lincoln had 2 well-documented periods of depression (or melancholia as it was called then). During these 2 periods, each lasting several months, he was taken in by relatives on a farm in Kentucky where someone was always with him to keep him from throwing himself into the river.

But everyone has moods and some must be worse than others. Why do we say that clinical forms of depression, namely major depression and bipolar disorder are brain diseases? As defined in Webster's dictionary, a disease is a set of clinical symptoms that are directly attributable to an abnormal body part (called pathology). The part of the brain that is malfunctioning in depression is not a single spot but a set of circuits in the brain in the frontal areas that are known because of both modern brain imaging methods show this (Mayberg et al , 2005; Drevets et al, 1997; House et al, 2000) but also from the known brain lesions of Parkinson's Disease and of stroke. Over half of patients with Parkinson's disease (which injures the basal ganglia in the subcortical regions of the frontal lobes) experience episodes of depression after their Parkinson's disease onsets and in stroke patients; the likelihood of clinical depression in the immediate aftermath is related to which area of the brain is injured by the stroke. Most cases of depression though are not caused by direct injuries to the brain, but by a combination of genetic and environmental factors that affect the structure and function of key circuits in the frontal areas of the brain. In this sense, depression is like asthma, it's largely genetic in origins but its exacerbations are usually caused by changes in the environment. For asthma patients this is often dust or pollen while for depressed patients psychological stressors are the most frequent environmental triggers. For asthma patients, when a severe attack occurs, removal of the dust or pollen is not sufficient therapy; medical treatment is needed to bring the patient back to normal breathing. Severe depression it is the same, the patient will need counseling and medications usually to achieve a remission sufficient to return to functioning. And longer term treatment between episodes is needed for many patients with asthma and with depression. Because we cannot as physicians control the flow of pollen or psychological stresses (which by themselves are not bad things for most people) it is important that we find the genes whose malfunction is ground zero on the pathway to these diseases. In depression because we don't understand why our medications help when they do help and why they fail in other cases, we need the molecular clues that genes can provide to make our treatments more effective. Genes which are molecules of DNA direct cells to make particular proteins. The proteins make up the structure of brain cells, brain pathways and circuits, and when they malfunction they make the brain vulnerable to stresses which can set off episodes of psychiatric

illnesses such as depression. Understanding how this works can't help but make us better at making diagnoses and giving the right treatments to the right patients. The molecular formulas should tell us much about which patients will respond to which of today's treatments and which will not. They should also guide us to create new treatments which would be "engineered" rationally based on knowledge of what is wrong in the brain, not just in the emotions or behavior of the patient.

Depression and bipolar disorders are common diseases like cancer and like cancer they have many different forms caused by several different genes and several distinct environmental toxins acting in combination. Like cancer, therefore, the big breakthroughs will not be cheap or easy and we can expect challenges at many steps. The War on Cancer was the right decision by Congress at the right time (1971) and it has led to a great deal of progress so that cancer deaths are finally falling and many forms of cancer are now detected early and cured and even severe cancers can be managed much better than they were 35 years ago. The key breakthrough that made the war on cancer possible was the discovery of the genetic code (called codons) which allowed pathologists who looked at tumors under the microscope see where the cellular mechanisms went astray, in the DNA, the RNA, or at the protein level itself. Thus pathologists and cancer experts could "interrogate" the tumors. However this technology was not sufficient to allow us to interrogate the living brain. Now with the genome project largely completed and the brain imaging methods progressing (and incorporating the imaging of proteins in the brain) we can now see how we might look into the mechanisms of depression like we have illuminated so much of the pathway to various forms of cancer. And as we have done with cancer patients, we now are much better at predicting which patients will respond to old treatments (radiation and hormonal manipulations) and we have also devised many new treatment strategies (immune therapies and new less toxic chemotherapies) that we never imagined before the molecular war on cancer was begun.

This description of depression (and Bipolar disorder) as today's "cancer" is very appropriate. When I started medical school at Johns Hopkins in 1968, there were only 4

cancer doctors on the staff. Cancer was a word that many doctors would not utter to their patients with cancer for fear of the stigma. Patients who were admitted with late “metastatic” cancers were often put in the room farthest from the doctors and nurses, not because the doctors or nurses didn’t like them, but because they didn’t know what to say and they thought there was nothing useful that they could do. Today, we understand cancer and although it is still a serious and often fatal condition there is no sense of cancer as a death sentence or as a stigma on the family whose relative suffers from it. At Johns Hopkins now there are over 200 cancer doctors and now 3 cancer buildings, reflecting the progress and the optimism we have about further progress in cancer. It has not been cheap or easy going. Cancer has not been eradicated and may never be fully eradicated but no one can deny the progress and the difference it has made to patients, families, and to society. We understand it so much better and, therefore, we are continuing to find new ways to prevent it, to detect it early, to cure it, and to make life meaningful and substantial as we manage some forms of it now as a chronic disease rather than as a death sentence.

The World Health Organization global burden of disease study has demonstrated that depression is the leading cause of disability world wide and that 5 of the top ten causes of disability are psychiatric disorders (depression, alcoholism, bipolar disorder, obsessive compulsive disorder, and schizophrenia). It has predicted that by 2020 depression will be “the second most debilitating disease worldwide, after ischemic heart disease, and one of the leading causes of death, as suicide takes more lives than traffic accidents, lung disease, or AIDS.” Cardiovascular disease receives the largest amount of government funding, 25 percent; diabetes gets about 8 percent and cancer a little over 6 percent, while all mental illnesses (which includes all of the conditions noted by the W.H.O. and many more) receives only 4 percent.

Of those who suffer from depression year, approximately 74% (or 7.8 million) of them are in the workforce. This has numerous implications as far as the potential strength of our economy, should this group of individuals have access to the mental

health care they require. Furthermore, workers with depression have a much higher rate of missed days than their healthy counterparts. On average, depression accounts for a 2.5 fold increase in the probability of missing work as a result of their illness (Langlieb and Kahn 2005). In 2000, depression alone was estimated to cost the US economy \$83.1 billion each year, most of it due to absenteeism and decreased productivity at work (Greenberg et al 2003).

The issue of mental health care is particularly timely as our nation is in the midst of the War on Terrorism. The primary goal of terrorism is not simply kill Americans, which can be done only on a small scale by our adversaries. The goal is to wage psychological war that will sap our citizen's morale and confidence in our civilization. Although depression and many forms of anxiety disorders have strong genetic components they also have strong environmental triggers. The events of September 11, 2001 created an enormous amount of mental anguish for those working in and living around the World Trade Center and the Pentagon. Numerous studies were published soon after these events describing both civilian and military response to these unspeakable attacks. Among of the 1008 adults randomly telephoned who reside near the World Trade Center, "9.7 percent reported symptoms consistent with current depression" (Galea et al 2002: 982). In a study on civilian and military employees of the Pentagon, 17.7 percent of respondents reported depressive symptoms following the attack events of 9/11 (Jordan et al 2004). This rate is higher when you examine the experiences of military personnel returning from the war in Iraq. When examined for mental health following deployment to Iraq, 19.1 percent of those questioned screened positive for depression (Hoge et al 2006). These numbers indicate a strong need for mental health care among those indirectly and directly affected by the events on and following September 11, 2001. It should be noted, as well, that a recent article in the New York Times reported an epidemic of depression and post-traumatic stress disorders in New Orleans following Hurricane Katrina. This mental health epidemic has lead to a three-fold increase in the suicide rate from that before the hurricane (Saulny 2006). Lack of resources in this area is compounding the problem and greatly taxing local mental health experts.

The need for research on disorders of mood disorders (and the other mental disorders as outlined by Dr Insel) is vital for our troops and to all American citizens. About 15 million people (10 million women and 5 million men) in the United States at any given time have major depression or some form of manic depression. The prevalence for depression runs very high, as do the costs to the individual and the country as a whole. It is imperative that we invest more time and money towards this “Cancer of the 21st Century,” so that treatments can lead to cures and hopes into reality.

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